Citation:

Bazzano LA, Li TY, Joshipura KJ, Hu FB. Intake of fruit, vegetables, and fruit juices and risk of diabetes in women. *Diabetes Care* 2008;(31)7:1311-1317.

PubMed ID: <u>18390796</u>

Study Design:

Prospective Cohort Study

Class:

B - <u>Click here</u> for explanation of classification scheme.

Research Design and Implementation Rating:



POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this study was to examine the association between fruit, vegetable, and fruit juice intake and development of type 2 diabetes mellitus.

Inclusion Criteria:

- Women enrolled in the Nurses' Health Study
- 121,700 female registered nurses between the ages of 30 and 55 years from 11 different U.S. states.

Exclusion Criteria:

- Those who left 12 or more food items blank on the questionnaire
- Women who died before the return of the 1984 questionnaire
- Diagnosis of cardiovascular disease, cancer, or diabetes at the 1984 assessment and those who were missing the diagnosis of diabetes

Description of Study Protocol:

Recruitment

- Registered nurses between the ages of 30 and 55 years from 11 different US states initially recruited into the Nurses' Health Study in 1976 through their response to an initial mailed questionnaire
- The diet cohort was established in 1980 with 98,462 participants.

Design: Prospective Cohort Study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis

- Participants were divided into quintiles by frequency of intake to avoid assumptions about the shape of the dose-response relationship.
- Cox proportional hazards models with time-dependent variables were used to adjust for potential confounders including BMI, family history of diabetes, smoking, postmenopausal hormone use, alcohol intake, and physical activity.
- The authors also adjusted for dietary variables that have been related to diabetes in the study cohort, including intakes of processed meats, potatoes, nuts, coffee, soda and whole grains.
- The proportional hazards assumption was tested by modeling the interaction of time with fruit and vegetable intake.
- To assess the linearity of trends, median values of intake for quintiles were treated as continuous in Cox regression models.

Data Collection Summary:

Timing of Measurements

- FFQ were evaluated every 4 years over an 18 year span of time (1980 to 1998).
- A semiquantitative food-frequency questionnaire (FFQ) was included in the general health questionnaire in 1980, 1984, 1986, 1990, 1994 and 1998.
- The 1984 FFQ was considered the baseline because the FFQ was unchanged afterwards.

Dependent Variables

- Development of type 2 diabetes based on self-report.
- At each 2 year cycle, participants were asked whether they had a diagnosis of diabetes. For each self-reported diagnosis of diabetes, a supplemental questionnaire was sent, asking about diabetes symptoms, diagnostic tests and treatments.
- The criteria for the diagnosis of diabetes was consistent with those proposed by the National Diabetes Data Group prior to 1997 and after 1998 the American Diabetes Associations' criteria.

Independent Variables

- Intake of fruits, vegetables and fruit juices
- Participants were asked to report the frequencies of their consumption of fruit and vegetable items during the previous year. For each fruit and vegetable a standard unit or portion size was specified. Nine responses were possible, ranging from "never" to "six or more times per day".
- The response to each food item was converted to average daily intakes and then summed to compute the total intake.

Control Variables

- Intakes of processed meats, potatoes, nuts, coffee, soda and whole grains
- Data on body mass index (BMI), physical activity, smoking status, alcohol use, postmenopausal hormone therapy, family history of diabetes, and physician-diagnosed

hypertension and high cholesterol were self-reported on biennial questionnaires

• BMI was calculated by using updated weight information for each time period.

Description of Actual Data Sample:

Initial N: Diet cohort established in 1980 with 98,462 participants

Attrition (final N): 71,346 remained after application of exclusion criteria

Age: 30 - 55 years at start of study (1976)

Ethnicity: not stated

Other relevant demographics: not stated

Anthropometrics

Location: 11 states in United States

Summary of Results:

Key Findings:

- Over the 18 years of follow-up (1,203,994 person-years), 4,529 cases of type 2 diabetes were documented
- Cumulative incidence of diabetes was 7.4%
- No association between total fruit and vegetable intake and risk of diabetes was identified in the age-adjusted or multivariate-adjusted models.
- For an increase of 3 servings/day in total fruit and vegetable consumption, the multivariate-adjusted hazard ratio was 0.99 (95% CI 0.94 1.05)
- For an increase of 3 servings/day in whole fruit consumption, the multivariate-adjusted hazard ratio was 0.82 (95% CI 0.72 0.94)
- Results were similar for the intake of total vegetables.
- Intake of total fruit and green leafy vegetables was inversely associated with development of type 2 diabetes.
- \bullet For an increase of 1 serving/day of green leafy vegetables, the multivariate-adjusted relative risk was 0.91 (95% CI 0.84 0.98, P < 0.01)
- For an increase of 1 serving/day of fruit juice, the multivariate-adjusted relative risk was 1.18 (95% CI 1.10 1.26; P < 0.001), demonstrating an association with increased hazard of diabetes

Author Conclusion:

Consumption of green leafy vegetables and fruit was associated with a lower hazard of diabetes, whereas consumption of fruit juices may be associated with an increased hazard among women.

Reviewer Comments:

Large number of participants, based on Nurses' Health Study. Several FFQs over 18 year

Research Design and Implementation Criteria Checklist: Primary Research					
Rele	evance Question	ns			
	1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes		
	2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes		
	3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes		
	4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes		
Vali	idity Questions				
1.	Was the res	earch question clearly stated?	Yes		
	1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes		
	1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes		
	1.3.	Were the target population and setting specified?	Yes		
2.	Was the sele	ection of study subjects/patients free from bias?	Yes		
	2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes		
	2.2.	Were criteria applied equally to all study groups?	Yes		
	2.3.	Were health, demographics, and other characteristics of subjects described?	No		
	2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes		
3.	Were study groups comparable?				
	3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A		
	3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A		

	3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
	3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
	3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
	3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method	d of handling withdrawals described?	Yes
	4.1.	Were follow-up methods described and the same for all groups?	Yes
	4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
	4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
	4.4.	Were reasons for withdrawals similar across groups?	Yes
	4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blindin	g used to prevent introduction of bias?	Yes
	5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
	5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
	5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
	5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
	5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.		vention/therapeutic regimens/exposure factor or procedure and rison(s) described in detail? Were interveningfactors described?	Yes
	6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A

	6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
	6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
	6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
	6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
	6.6.	Were extra or unplanned treatments described?	N/A
	6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
	6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcor	nes clearly defined and the measurements valid and reliable?	Yes
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the stat outcome ind	istical analysis appropriate for the study design and type of icators?	Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes

	8.6.	Was clinical significance as well as statistical significance reported?	Yes	
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A	
9.	. Are conclusions supported by results with biases and limitations taken int consideration?			
	9.1.	Is there a discussion of findings?	Yes	
	9.2.	Are biases and study limitations identified and discussed?	Yes	
10.	10. Is bias due to study's funding or sponsorship unlikely?		Yes	
	10.1.	Were sources of funding and investigators' affiliations described?	Yes	
	10.2.	Was the study free from apparent conflict of interest?	Yes	

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